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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,548	03/07/2006	Maria Jose Fernandez	4258-116	9386

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RESEARCH TRIANGLE PARK, NC 27709

EXAMINER

WESTERBERG, NISSA M

ART UNIT	PAPER NUMBER
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1618

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02/23/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,548	Applicant(s) FERNANDEZ ET AL.	
	Examiner Nissa M. Westerberg	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 - 10, 12 - 21, 23 - 33 is/are pending in the application.
- 4a) Of the above claim(s) 1 - 10, 12 - 15, 21, 23 - 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16 - 20, 29 - 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed December 10, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 16 - 20 and 31 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 - 12 of copending Application No. 12/301835. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed June 10, 2009 and those set forth below.

Applicants request that this rejection be deferred pending identification of allowable claims. Therefore, this rejection is maintained for the reasons of record.

Response to Amendment

3. The declaration under 37 CFR 1.132 filed December 10, 2009 is sufficient to overcome the rejection of claims 6 - 20, 22 and 29 - 31 based upon 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 16 - 20 and 29 – 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation “characterized by a stability of at least one month at ambient temperature storage” is indefinite. It is not clear what parameter(s) are used as the basis of the stability determination and the level of change, if any, that could occur in that parameter that would result in an unstable composition.

While claims 32 and 33 recite the physical properties of particle size and zeta potential, these are also indefinite as the accepted level of change in these parameters is not defined.

As the meaning of this phrase is indeterminate, the Examiner is unable to determine whether or not this claim limitation meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 16 – 20 and 29 – 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prokop et al. (US 2003/0170313) in view of Calias et al. (US 2003/0087877). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed June 23, 2008, January 2, 2009 and June 10, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that there is no derivative basis in Prokop for the nanoparticles of applicant's claimed invention. Attention is directed towards example 4 and the Rule 1.132 declaration for empirical evidence of the surprisingly improved stability resulting from the presence of a hyaluronic acid salt. This advantage is not derivable from the combination of Prokop and Calias as there is nothing in either reference that would have caused one of ordinary skill in the art to utilize a hyaluronic acid salt in order to achieve the surprisingly enhanced stability. Citing *KSR Intl Co. v. Teleflex*, Applicant states that just because references can be combined or modified does not render the combination obvious unless the results would have been predictable. Calias et al. uses hyaluronic acid as a solid biomaterial and utilizes covalent bonds to attach a therapeutic agent to the hyaluronic acid. There is no indication in Calias that the hyaluronic acid could be used as an anionic component in the formulation of Prokop. As the instant claims state that there are no covalent bonds between the hyaluronic acid salt, cationic polymer, polyanionic salt and active ingredient, Calias teaches away from the claimed invention by teaching a covalently bonded component. In conjunction with the unexpected and surprisingly improved stability, the instant claims are patentable.

In regards to the new limitations regarding the stability of the particles, the nanoparticles taught by the combination of Prokop and Calias have the same composition and ingredients as recited by the instant claims. The same compositions must have the same properties. Therefore, the nanoparticles of Prokop and Calias must necessarily have the same stability. The instant claims are product by process claims. If

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this stability arises from the method by which the particles are produced, Applicants must show evidence as to the different nature of the products obtained by the different processes. “As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.” **MPEP 2113**

Applicants arguments are unpersuasive. In order to overcome a *prima facie* case of obviousness, it is incumbent upon the Applicant to provide comparative test evidence that demonstrates unexpected superiority of the claimed compositions versus the closest prior art compositions, and not simply an advantage predictable from the prior art. See *In re Chapman*, 148 USPQ 711, 715 (CCPA, 1966). Moreover, such proffered comparisons must be commensurate in scope with the breadth of the claims. See *In re Clemens*, 206 USPQ 289, 296 (CCPA, 1980) and *In re Coleman*, 205 USPQ 1172, 1175 (CCPA 1980).

The data provided by the Applicant does not provide comparative evidence for any formulations that use something other sodium hyaluronate, such as the formulations disclosed in Prokop that utilize other polyanionic polymers in the formation of nanoparticles. Also, the data presented relate to only three different cationic polymers – cationic collagen, gelatin and chitosan. There is no explanation or indication that the results obtained for these specific cationic polymers are generalizable to the entire genus of “cationic polymers”. There is no explanation or indication that the results obtained for nanoparticles prepared from sodium hyaluronate are generalizable to the full genus of “hyaluronic acid salts”. There is no explanation or indication that the result

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obtained from the specific ratios of these ingredients are generalizable to any proportion of the hyaluronic acid salt and cationic polymer and sodium triphosphate, the full breadth of the claim.

As evidence of the unexpected superior properties of the nanoparticles commensurate in scope with the instant claims and comparing the instant products prepared by the instant process to the closest cited prior art has not been presented, this line of argument is unpersuasive.

Prokop generally teaches that nanoparticle prepared using a mixture of polyanionic polymers and polycations and Calias et al. teaches that hyaluronic acid salts and polyanionic polymers. Thus, one of ordinary skill in the art would have a reasonable expectation of success in preparing nanoparticles with the claimed composition. The properties of the prepared particles, and the alleged improvement of stability is a secondary consideration, which was discussed in greater detail above.

In regards to the teaching away argument, “the prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed....” *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). **MPEP 2123**, emphasis added. Prokop discloses that covalent attachment of the therapeutic (active) ingredient is not required. Whether or not the active agent is covalently attached will alter the release profile of the active agent but does not rise to the level of teaching away from the non-covalent association of the various components.

Therefore, this rejection is maintained. As there is no allowable subject matter, the request for rejoinder is denied.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW